S/N 09/458,862 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant:	Allison Hubel	Examiner: Elli Peselev
Serial No.:	09/458,862	Group Art Unit: 1623
Filed:	December 10, 1999	Docket: 600.451US1
Title:	COMPOSITIONS AND METHODS FOR CRYOPRESERVATION OF PERIPHERAL BLOOD LYMPHOCYTES	

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On February 9, 2004, Appellant submitted a Rule 116 Amendment (copy enclosed) and a Reply Brief, as evidenced by the copy of the corresponding date stamped postcard enclosed herewith. In that Amendment claims 1-2, 6, 14, 20, 26, 30-31, 37, and 53-58 were amended, claims 59-60 were added, and claims 35-36 were canceled. The Examiner is requested to note that the present Amendment was referred to in Appellant's Brief on Appeal mailed September 24, 2003 (see Section 4), and the claims therein were argued in the Brief and were included in Appendix I of that Brief. It is Appellant's position that the amended claims are in better form for appeal.

For instance, the amendment to claims 1-2, 14, 26, 30-31, 37, and 53-58 addressed the 35 U.S.C. § 112, second paragraph, rejection of claims 1-8, 11-12, 14, 16-17, 19-22, 24, 26-28, 30-44, and 47-58 over the phrase "lymphocytes modified *ex vivo*". The amendment to claims 14 and 31 (both in Group I) to recite "wherein the arabinogalactan, biological or functional equivalent thereof, in the medium results in a high post-thaw survival rate for the freshly isolated lymphocytes, hematopoietic stem cells, or lymphocytes which are activated or genetically modified *ex vivo*" provides consistency to the claims in Group I (note that independent claims 1, 53 and 55, which are also in Group I, already recited this phrase). The amendments to claims 26 and 58 (both in Group II) provide consistency to and correct grammatical errors in those claims. The amendments to claims 6, 14, 20, 54, 56, and 57 correct grammatical errors, e.g., the insertion of "the" or "and glycerol" or the deletion of "or a".

Pursuant to a request by the Examiner, a revised Appendix I: Claims On Appeal, which does not include the amendments referred to above, is included herewith.

Respectfully submitted,

ALLISON HUBEL,

By her Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 373-6959

Date April 15, 2004 By _____
Janet E. Embretson
Reg. No. 39,665

I hereby certify that this paper is being transmitted by facsimile to the U.S. Patent and Trademark Office on the date shown below.

Dawn M. Poole

Dawn M. Poole

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APPENDIX I: The Claims on Appeal

1. A cryopreservation medium comprising a balanced electrolyte solution incorporating at least one cryoprotective agent that is arabinogalactan, or a biological or functional equivalent thereof, which agent is present in an amount of 1% w/v to 40% w/v, and freshly isolated lymphocytes, hematopoietic stem cells, lymphocytes which are modified *ex vivo*, or a combination thereof, wherein the medium does not comprise dimethylsulfoxide or serum, and wherein the arabinogalactan, a biological or functional equivalent thereof, in the medium results in a high post-thaw survival rate for the freshly isolated lymphocytes, hematopoietic stem cells, or lymphocytes which are modified *ex vivo*.

2. The cryopreservation medium of claim 1 wherein the cells are peripheral blood lymphocytes.

3. The cryopreservation medium of claim 1 that comprises arabinogalactan.

4. The cryopreservation medium of claim 1 further comprising a cryoprotective agent that penetrates the cell membrane.

5. The cryopreservation medium of claim 4 wherein the cryoprotective agent that penetrates the cell membrane is glycerol or propylene glycol.

6. The cryopreservation medium of claim 1 further comprising a cryoprotective agent other than arabinogalactan or a biological or functional equivalent thereof which does not penetrate the cell membrane.

7. The cryopreservation medium of claim 1 which does not comprise protein.

8. The cryopreservation medium of claim 1 which is infusible.

11. The cryopreservation medium of claim 1 wherein the cells are human cells.

12. The cryopreservation medium of claim 1 wherein the cells are non-human vertebrate cells.

14. A composition suitable for administration to a human, comprising a suspension of cells in a cryopreservation medium comprising a balanced electrolyte solution incorporating at least one cryoprotective agent that is arabinogalactan, or a biological or functional equivalent thereof, and a cryoprotective agent that penetrates the cell membrane, wherein arabinogalactan, or a biological or functional equivalent thereof, is present in an amount of 1% w/v to 40% w/v, wherein the cells are freshly isolated lymphocytes, hematopoietic stem cells, lymphocytes which are modified *ex vivo*, or a combination thereof,

and wherein the medium does not comprise dimethylsulfoxide or serum.

16. The composition of claim 14 wherein the cells are peripheral blood lymphocytes.

17. The composition of claim 14 wherein at least one of the cryoprotective agents is arabinogalactan.

19. The composition of claim 14 wherein the cryoprotective agent that penetrates the cell membrane is glycerol or propylene glycol.

20. The composition of claim 14 further comprising a cryoprotective agent other than arabinogalactan or a biological or functional equivalent thereof which does not penetrate the cell membrane.

21. The composition of claim 14 which does not comprise protein.

22. The composition of claim 14 which is infusible.

24. The composition of claim 14 wherein the cells are human cells.

26. A method for preserving cells comprising:

(a) contacting cells with a cryopreservation medium comprising a balanced electrolyte solution and at least one cryoprotective agent that is arabinogalactan, or a biological or functional equivalent thereof, in an amount of 1% w/v to 40% w/v, to yield a cell suspension, wherein the cells are freshly isolated lymphocytes, hematopoietic stem cells, lymphocytes which are modified *ex vivo*, or a combination thereof, wherein the medium does not comprise dimethylsulfoxide or serum, and wherein the arabinogalactan in the medium results in a high post-thaw survival rate for the freshly isolated lymphocytes, hematopoietic stem cells, or lymphocytes which are modified *ex vivo*; and

(b) freezing the cell suspension to yield a frozen cell suspension.

27. The method of claim 26 further comprising thawing the frozen cell suspension under conditions that maintain cell viability.

28. The method of claim 26 wherein the cells are human cells.

30. The method of claim 26 wherein the cells are peripheral blood lymphocytes

31. A frozen composition comprising i) a balanced electrolyte solution, ii) at least one cryoprotective agent that is arabinogalactan, or a biological or functional equivalent thereof, in an amount of 1% w/v to 40% w/v, and iii) freshly isolated lymphocytes, hematopoietic stem cells, lymphocytes which are modified *ex vivo*, or a combination thereof, wherein the composition does not comprise dimethylsulfoxide or serum.

32. A frozen hematopoietic cell-containing composition made according to the method of claim 26.

33. The cryopreservation medium of claim 5 wherein the cryoprotective agent that penetrates the cell membrane is glycerol.

34. The cryopreservation medium of claim 33 wherein the concentration of glycerol is about 1% to about 3%.

35. The cryopreservation medium of claim 1 wherein the lymphocytes which are modified *ex vivo* are activated lymphocytes or genetically modified lymphocytes.

36. The composition of claim 14 or 31 wherein the lymphocytes which are modified *ex vivo* are activated lymphocytes or genetically modified lymphocytes.

37. A cryopreservation medium comprising a balanced electrolyte solution, at least one cryoprotective agent that is arabinogalactan, or a biological or functional equivalent thereof, in an amount of 1% w/v to 40% w/v and freshly isolated lymphocytes, hematopoietic stem cells, lymphocytes which are modified *ex vivo*, or a combination thereof, wherein the medium does not comprise dimethylsulfoxide or serum, and wherein the balanced electrolyte solution is selected from the group consisting of lactated Ringer's solution, PlasmaLyte-A™, Normosol-R™, Veen-D™, Polysal®, and Hank's balanced salt solution.

38. The cryopreservation medium of claim 37 wherein the lymphocytes are peripheral blood lymphocytes.

39. The cryopreservation medium of claim 37 wherein the agent is arabinogalactan.

40. The cryopreservation medium of claim 37 further comprising a cryoprotective agent that penetrates the cell membrane.

41. The cryopreservation medium of claim 40 wherein the cryoprotective agent that penetrates the cell membrane is glycerol or propylene glycol.

42. The cryopreservation medium of claim 37 further comprising a

cryoprotective agent other than arabinogalactan or a biological or functional equivalent thereof which does not penetrate the cell membrane.

43. The cryopreservation medium of claim 37 which does not comprise protein.

44. The cryopreservation medium of claim 37 which is infusible.

47. The cryopreservation medium of claim 37 wherein the cells are human cells.

48. The cryopreservation medium of claim 37 wherein the cells are non-human vertebrate cells.

49. The method of claim 26 wherein the medium comprises arabinogalactan.

50. The method of claim 26 further comprising a cryoprotective agent that penetrates the cell membrane.

51. The method of claim 50 wherein the cryoprotective agent that penetrates the cell membrane is glycerol or propylene glycol.

52. The method of claim 26 wherein the lymphocytes which are modified *ex vivo* are activated lymphocytes or genetically modified lymphocytes.

53. A cryopreservation medium comprising a balanced electrolyte solution incorporating at least one cryoprotective agent that is arabinogalactan, which is present in an amount of 1% w/v to 40% w/v, and freshly isolated lymphocytes, hematopoietic stem cells, lymphocytes which are modified *ex vivo*, or a combination thereof, wherein the medium does not comprise dimethylsulfoxide or serum, and wherein the arabinogalactan in the medium results in a high

post-thaw survival rate for the freshly isolated lymphocytes, hematopoietic stem cells, or lymphocytes which are modified *ex vivo*.

54. A cryopreservation medium comprising a balanced electrolyte solution incorporating at least one cryoprotective agent that is arabinogalactan, which is present in an amount of 1% w/v to 40% w/v, glycerol in amount of 0.5% to about 20%, and freshly isolated lymphocytes, hematopoietic stem cells, lymphocytes which are modified *ex vivo*, or a combination thereof, wherein the medium does not comprise dimethylsulfoxide or serum, and wherein the the arabinogalactan in the medium results in a high post-thaw survival rate for the freshly isolated lymphocytes, hematopoietic stem cells, or lymphocytes which are modified *ex vivo*.

55. A frozen composition comprising i) a balanced electrolyte solution, ii) at least one cryoprotective agent that is arabinogalactan in an amount of 1% w/v to 40% w/v, and iii) freshly isolated lymphocytes, hematopoietic stem cells, lymphocytes which are modified *ex vivo*, or a combination thereof, wherein the composition does not comprise dimethylsulfoxide or serum, and wherein the arabinogalactan in the composition results in a high post-thaw survival rate for the freshly isolated lymphocytes, hematopoietic stem cells, or lymphocytes which are modified *ex vivo*.

56. A frozen composition comprising i) a balanced electrolyte solution, ii) at least one cryoprotective agent that is arabinogalactan in an amount of 1% w/v to 40% w/v, iii) glycerol in amount of 0.5% to about 20%, and iv) freshly isolated lymphocytes, hematopoietic stem cells, lymphocytes which are modified *ex vivo*, or a combination thereof, wherein the composition does not comprise dimethylsulfoxide or serum, and wherein the arabinogalactan in the composition results in a high post-thaw survival rate for the freshly isolated lymphocytes, hematopoietic stem cells, or lymphocytes which are modified *ex vivo*.

57. A method for preserving cells comprising: freezing a cell suspension comprising cells and a cryopreservation medium comprising a balanced electrolyte solution, arabinogalactan in an amount of 1% w/v to 40% w/v, and glycerol in amount of 0.5% to about 20%, to yield a cell suspension, wherein the cells are freshly isolated lymphocytes, hematopoietic stem cells,

lymphocytes which are modified *ex vivo*, or a combination thereof, wherein the medium does not comprise dimethylsulfoxide or serum, and wherein the arabinogalactan in the medium results in a high post-thaw survival rate for the freshly isolated lymphocytes, hematopoietic stem cells, or lymphocytes which are modified *ex vivo*.

58. A method for preserving cells comprising:

(a) contacting cells with a cryopreservation medium comprising a balanced electrolyte solution and at least one cryoprotective agent that is arabinogalactan, in an amount of 1% w/v to 40% w/v, to yield a cell suspension, wherein the cells are freshly isolated lymphocytes, hematopoietic stem cells, lymphocytes which are modified *ex vivo*, or a combination thereof, and wherein the medium does not comprise dimethylsulfoxide or serum; and

(b) freezing the cell suspension at a cooling rate of about 1° to about 10° C/minute to yield a frozen cell suspension.